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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,175	08/07/2002	Michael J. Daly	044508-5003US	9734
9629	7590	10/20/2006		EXAMINER PAK, YONG D
MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004			ART UNIT 1652	PAPER NUMBER

DATE MAILED: 10/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action Before the Filing of an Appeal Brief</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/089,175	DALY ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Yong D. Pak	1652

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 September 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
  - a)  The period for reply expires 3 months from the mailing date of the final rejection.
  - b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2.  The Notice of Appeal was filed on 27 August 2006. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
  - (a)  They raise new issues that would require further consideration and/or search (see NOTE below);
  - (b)  They raise the issue of new matter (see NOTE below);
  - (c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5.  Applicant's reply has overcome the following rejection(s): see attached.
6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1,2,6,12,25-28 and 42-53.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.
13.  Other: \_\_\_\_\_.

## **ADVISORY ACTION**

This application is a continuation of PCT/US00/26504.

Claims 1-2, 6, 12, 25-28 and 42-53 are pending and are under consideration.

### ***Response to Arguments***

The amendment filed on September 1, 2006 under 37 CFR 1.116 in reply to the final rejection will be **ENTERED** and has been considered but is not deemed to place the application in condition for allowance because: the amendment and request for consideration does not overcome the rejections of claims 1-2, 6, 12, 25-28 and 42-53 under 35 U.S.C. 112, 1<sup>st</sup> paragraph, 2<sup>nd</sup> paragraph and 103(a), as discussed below.

### ***Withdrawn Claim Rejections - 35 USC § 112***

Previous rejection of claim 6 under 35 U.S.C. 112, second paragraph, for depending on a canceled claim, is withdrawn in light of the amendment of claim 6.

Previous rejection of claims 1 and 52-53 and claims 2, 12, 25-28 and 42-51 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, for the recitation of "capable of detoxifying", is withdrawn in light of the amendment deleting said phrase from said claims.

Previous rejection of claims 42 and 53 are rejected under 35 U.S.C. 112, first paragraph, for new matter, is withdrawn by virtue of Applicant's pointing to specific support for the alleged new matter.

***Maintained Claim Rejections - 35 USC § 112 & 35 USC § 103***

Claims 47 and 49-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants argue that based on the common knowledge and the dictionary definition of the term, one of skill in the art would know the meaning of this phrase. Examiner respectfully disagrees. Literally, the term "derivative" means a substance that can be made from another substance. Therefore, it is not clear to the Examiner either from the specification or form the claims as to what applicants mean by the above phrase or the metes and bounds of the claimed plasmids.

Hence the rejection is maintained.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants argue that since the specification teaches advantageous proteins, the claim is not indefinite. Examiner respectfully disagrees. The metes and bounds of this phrase in the context of the claims are not clear to the Examiner. It is not clear to the

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Examiner either from the specification or form the claims as to what proteins are encompassed by the above phrase.

Hence the rejection is maintained.

Claims 1-2, 12, 25-28 and 43-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue the claims meet the written description requirement because the specification describes multiple species of Deinococcus bacterium containing a *mer* operon. Examiner respectfully disagrees. The claims are not limited to *Deinococcus radiodurans* transformed with a specific *mer* operon, but the claims are drawn to *D. radiodurans* bacteria transformed with a genus comprising any or all *mer* operon, including any or all mutants, variants and recombinants thereof, wherein the resulting transformed bacteria detoxifies a genus comprising any or all heavy metals. The specification, however, only discloses a single species, *D. radiodurans* transformed with a specific *mer* operon as described in Example 2, wherein the transformed bacterium detoxifies a single heavy metal, mercury. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying

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characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case, the claims are drawn to *Deinococcus radiodurans* bacteria transformed with a genus comprising a *mer* operon having any structure, including any or all mutants, variants and recombinants thereof, wherein the resulting bacteria detoxifies a genus comprising any or all heavy metals. The genus of the claims are structurally diverse as it encompasses any or all *mer* operon, wherein the resulting bacteria detoxifies any or all heavy metals. As such, neither the description of solely functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

Hence the rejection is maintained.

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Claims 42 and 49-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have requested that this rejection be held in abeyance as Applicants are in the process of obtaining the necessary deposit information. Hence the rejection is maintained.

Claims 1-2, 12, 25-28 and 43-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a radiation resistant *D. radiodurans* transformed to specifically express the mercuric reductase encoded by the *mer* operon (as in Example 2) that confers mercury resistance function to *E. coli*, such that the transformed bacteria is radiation resistant (ionizing radiation) and detoxifies mercury, does not reasonably provide enablement for *Deinococcus radiodurans*, transformed to any or all *mer* operon from any source, wherein the transformed bacteria detoxifies any or all heavy metals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants argue that claims meet the enablement requirement because *Deinococcus* bacterium are naturally transformable and the skilled artisan could readily transform the *mer* operon into any strain of *Deinococcus* without undue experimentation. Examiner respectfully disagrees. The claims are drawn to *D.*

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*radiodurans* transformed with any or all *mer* operon, including any or all mutants, variants and recombinants thereof, wherein the resulting bacteria detoxifies any or all heavy metals. The specification, however, only teaches a single species *D. radiodurans* transformed with a specific *mer* operon, wherein the transformed bacterium detoxifies a single heavy metal, mercury. As discussed above, predictability of which modifications can be tolerated by any or all *mer* operon that results in a radiation resistant bacteria that detoxifies heavy metals requires a knowledge and guidance with regard to which *mer* operon to use and how tolerant the bacteria and proteins encoded by the *mer* operon are to such modifications such that the modified bacterium continues to have said claimed activity. It is this specific guidance that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making and testing each of the enormously large number of mutants that results from such experimentation.

Hence the rejection is maintained.

Claims 1-2, 12, 25-28 and 42-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamlett et al. and Daly et al.

Applicants argue that the same claims have been rejected for both being obvious and lacking enablement and that it is unclear to applicants how the skilled artisan would find such claims lacking enablement if it would be obvious to the skilled artisan to reproduce the claims without undue experimentation. Examiner respectfully disagrees with such an argument. The enablement rejection argues that applicants are

indeed enabled for the *D. radiodurans* transformed with the specific *mer* operon as in Example 2, but not enabled for such a bacterium transformed with any or all *mer* operon. Examiner has also shown that what is enabled is also obvious in the rejection under 35 USC 103(a). However, Examiner has not argued that it would be obvious to transform *D. radiodurans* using any *mer* operon and obtain a bacterium capable of detoxifying mercury. Therefore, contrary to applicants' argument, Examiner has not imposed an improper enablement and obviousness rejection.

Applicants also argue use of improper hindsight reasoning. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, it should be noted that the knowledge of transforming *D. radiodurans* with said genes was well known and within the level of one having ordinary skill in the art at the time the invention was made.

Applicants argue that the claims are non-obvious because Hamlett et al. fails to suggest or disclose the use of the *mer* operon in *Deinococcus* species, bacterial capable of withstanding high doses of ionizing radiation, use of the *mer* operon in the presence of radiation, use of the *mer* operon for bioremediation or a constitutive promoter for the *mer* operon. In response to applicant's arguments against the

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references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that the claims are non-obvious because Daly et al. fails to suggest or disclose use of the *mer* operon in its plasmids, use of *D. radiodurans* in bioremediation or *D. radiodurans* transformed with the *mer* operon in bioremediation and that Daly et al. does not teach that *D. radiodurans* with the *mer* operon is able to grow in the presence of continuous ionizing radiation. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that (1) one of ordinary skill in the art would not have been motivated to combine the *mer* operon into a plasmid of Daly et al. to transform *D. radiodurans* and Daly et al. and Hamlett et al. fails to suggest or provide any motivation that *D. radiodurans* could be used for bioremediation and (2) that there is no reasonable expectation of success of either using the *mer* operon in the plasmid of Daly et al. or using a *D. radiodurans* transformed with the *mer* operon for bioremediation, nor is there any reasonable expectation of success of using *D. radiodurans* transformed with a *mer* operon under control of a constitutive promoter. Examiner respectfully disagrees. (1) One of ordinary skill in the art would have been motivated to make a bacterium having

resistance to both radiation and mercury, for its application in detoxifying mercury contaminated radioactive wastes (bioremediation). (2) One of ordinary skill in the art would have had a reasonable expectation of success in expressing proteins encoded by the *mer* operon in *D. radiodurans* since Hamlett et al. teaches plasmids comprising said operon and Daly et al. teaches how to transform *D. radiodurans* with foreign polynucleotides using an autoreplication plasmid. Further, obviousness does not require absolute predictability. If applicants are aware of any evidence showing there was no reasonable expectation of success, applicants are urged to present them.

Hence the rejection is maintained.

Claims 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamlett et al. and Daly et al. as applied to claims 1-2, 12, 25-28 and 42-53 above, and further in view of Lin et al.

Applicants argue that since claims 25-28 are not obvious for the reasons set forth above, these claims are also not obvious. Examiner respectfully disagrees, as discussed above. Hence the rejection is maintained.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax

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phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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